REMARKS

As Applicants are merely cancelling the non-elected claims and Claim 70, without prejudice or disclaimer, and making a clarifying amendment to Claim 55, it is requested that this amendment be entered and considered at this time.

I. Allowable Subject Matter

Applicants appreciate the Examiner's allowance of Claims 1-54, 75-77 and 97-107.

II. Claim Amendments – Reference to Disclosure

As explained in depth below, while Applicants respectfully traverse the rejections in the August 13, 2004 Final Rejection, in order to advance the prosecution of this application, independent Claim 55 has been amended to more clearly claim the method for treatment recited in this claim. In particular, this claim is now more explicitly directed to treating tissue by scanning with a beam of light. This feature is clearly supported by the application as filed as explained below.

Examples in support of such claimed method of treatment by scanning with a beam of light are found throughout the specification of the present application. For instance, the present application describes treatment to promote thermal overload of pigmented tissue in the following terms:

> "A focused light beam ... is preferable where the location and extent of the lesion is precisely known, since improved control over the extent of the treatment zone is thereby possible. By *scanning* this focused light beam ... throughout the volume of the tumor, it is possible to treat the entirety of the pigmented tumor cells.... However, where the location and extent of the lesion is not precisely known, or where the lesion is exceptionally large, use of a non-focused light beam ... is

preferred to assure that treatment is effected in all of the pigmented tumor cells...."
(p. 25, lines 12 - 18, emphasis added)

Accordingly, this passage clearly defines the claimed treatment to include scanning with a beam of light (either focused or non-focused) in order to treat a volume of tissue.

Applicants have amended independent Claim 55 to better reflect these teachings, in particular with regard to the specific aspects of the application of light energy. In addition, Claim 70 has been canceled to eliminate any potential conflict with amended Claim 55. As shown *supra*, this amendment has not added any new matter and clarifies the claimed method of treatment of pigmented tissue disclosed by the present application.

Accordingly, for at least the above-stated reasons, it is respectfully submitted that this amendment to Claim 55 is supported by the application as filed. Therefore, it is requested that the amendment be entered and considered at this time.

Applicants will now address each of the Examiner's remaining rejections and comments in the order in which they appear in the Final Rejection.

III. Claim Rejections – 35 USC §102 (Latina)

In the Final Rejection, the Examiner rejects Claims 55-61, 64-65, 68-69 and 72-74 under 35 U.S.C. §102(e) as being anticipated by Latina (USP 5,549,596). This rejection is respectfully traversed for at least the following reasons. As explained in more depth below, Latina does not disclose or suggest the invention of amended independent Claim 55 of the present application.

For example, Latina does not disclose or suggest the scanning illumination of a volume of tissue as recited in independent Claim 55. Instead, Latina describes illumination of individual target

areas of tissue using a static laser beam. This is clear from a number of passages in Latina, including the following from Latina's Summary of the Invention:

> "In a preferred embodiment, the radiation is delivered in pulses.... The radiation may be delivered in a single pulse. In a further preferred embodiment, the laser radiation impinges upon the intraocular area in a target spot of between about 0.05 and about 1.5 mm in diameter." (col. 2, lines 10-14)

Thus, Latina is describing illumination of individual spots, not scanning over a volume of tissue, as in amended Claim 55. This static method of illumination is further illustrated by Figure 1, where Latina shows a very detailed apparatus for use in practicing the method disclosed in the reference (see col. 2, lns. 66-67) and that is only usable for static illumination.

Further evidence that Latina does not disclose scanning is shown wherein, Latina prescribes using a static, "large target spot," as indicated by the following passage from Latina's Detailed Description of Exemplary Embodiments:

> "The desired radiant exposure may be achieved by modifying the target spot size.... In general, *the target spot size is large compared to those utilized in many previous applications* of laser therapy to the eye; in preferred embodiments of the invention, the target spot size is from about 0.1 to about 1 mm in diameter. The large target spot size is possible because the method of the invention provides selective cell damage based on cell pigmentation, in contrast to prior art laser ablation methods, in which tissues are damaged nonselectively. For example, in prior techniques which ablate tissue by photodisruption, the high fluence which results in nonselective tissue ablation follows from the small target spot size, typically about 25 μm. It is a major advantage of the technique of the invention that focusing is not necessary to achieve selective killing.... A large target area is advantageous: *surgical time is minimized when the laser apparatus needs to be redirected fewer times*." (col. 3, line 49 - col. 4, line 1, emphasis added)

Thus, Latina teaches that a large target area (i.e., up to "about 1 mm in diameter") reduces surgical time because the apparatus is *redirected only a few times* to a few specific target areas. Clearly, such an approach (i.e., physically redirecting a static illumination spot a few times) is not comparable to

automated scanning of a treatment beam over a volume of tissue taught in the present application and the claimed scanning in amended Claim 55.

Hence, Latina clearly does not disclose and never considered the scanning approach of amended independent Claim 55 of the present application, and therefore cannot anticipate nor render obvious Claim 55 or those claims dependent thereon.

Therefore, for at least the above-stated reasons, Latina fails to disclose or suggest the method of amended independent Claim 55 of the present application. Accordingly, this independent claim and those claims dependent thereon are patentable over the cited reference, and it is respectfully requested that this rejection be withdrawn.

IV. Claim Rejections – 35 USC §102 (Aprile Carpenter)

The Examiner also rejects Claims 55-56, 60 and 71-74 under 35 U.S.C. §102(b) as being anticipated by Aprile Carpenter (EP 0 649 667 A2). This rejection is also respectfully traversed for at least the following reasons. As explained in more depth below, Aprile Carpenter does not disclose or suggest the invention of the amended claims of the present application.

First, Aprile Carpenter does not describe or suggest the claimed scanned illumination approach of independent Claim 55 of the present application. In fact, Aprile Carpenter teaches away from such scanning by requiring a special fiberoptic illumination device. This special illumination method and apparatus is described by the following passages from the reference:

> "[0056] The central feature, without which the proper delivery of Enhanced Hyperthermia *would not be possible,* and, at the same time one of several technological innovations in the LAILT System, is the presence of multiple fiberoptic guided beams of nearly identical power, originating from distinct individually driven

laser energy sources, which ensure uniform distribution of power within the illuminated region.

"[0057] The latter characteristic is *vital* for the certain acquisition of the target temperature (50 degrees Celsius) by tagged tissue only, as the only way to ensure its total necrosis."

"[0059] In other words, the present invention apparatus provides also a method for the generation of uniform and unfocused monochromatic laser light and irradiation by the same of an extended area." (cols. 6-7 of Aprile Carpenter; emphasis added)

Thus, Aprile Carpenter teaches that the method described in the reference cannot be practiced without use of the "LAILT System," which comprises a fiberoptic bundle for delivery of a uniform beam of light to a treatment region. The reference describes such system in great detail. Aprile Carpenter, however, does not describe any means or reasons for scanning with this beam.[1] Accordingly, Aprile Carpenter cannot anticipate nor render obvious the claimed subject matter of amended independent Claim 55 of the present application nor any claim dependent thereupon.

Second, in contrast to Claim 55, Aprile Carpenter requires use of an *exogenous pigment*, as described by the following passages from the reference:

"[0020] Selective targeting of only malignant tissue is achieved through the widely utilized standard method of neoplastic tissue tagging, followed by illumination with Quantum Energy, namely laser light of a wavelength not readily absorbed by live tissue, under normal circumstances."

"[0027] The actual bio-mechanism requires the intra venous injection of a chomophore carrying compound, which is non-toxic and does not causes any particular chemical reaction within the tissue, but simply delivers the stain to the general location." [cols. 3-4 of Aprile Carpenter]

---

[1] Applicants note that any attempt to scan with such a device would most likely degrade the highly uniform illumination field that is the central feature of the LAILT System, presumably negatively affecting the uniform distribution of power specified by Aprile Carpenter.

These passages make it clear that the method of Aprile Carpenter is only applicable to treatment of tissue into which an exogenous pigment has been administered (i.e., via the "standard method of neoplastic tissue tagging"). This method consists of "injection of a chromophore carrying compound" into such tissue. Claim 55 of the present application specifically recites use of an endogenous pigment. Accordingly, since the exogenous pigment of the reference is not an endogenous pigment, as required by independent Claim 55 of the present application, Aprile Carpenter cannot anticipate nor render obvious the subject matter of this claim or any claim dependent thereupon.

Therefore, for at least the above-stated reasons, Aprile Carpenter fails to disclose or suggest the method of amended independent Claim 55 of the present application. Accordingly, this independent claim and those claims dependent thereon are patentable over the cited reference, and it is respectfully requested that this rejection be withdrawn.

V. Claim Rejections – 35 USC §103 (Latina in view of Mourou)

In the Final Rejection, the Examiner also rejects Claims 62-63, 66-67 and 70 under 35 U.S.C. §103(a) as being unpatentable over Latina in view of Mourou (USP 5,656,186). This rejection is also respectfully traversed.

More specifically, in the Final Rejection, the Examiner combines the teachings of Latina and Mourou to arrive at this rejection. As a basis for this rejection, the Examiner alleges that "it would have been obvious to one of ordinary skill in the art to combine the teaching of a method of using a laser comprising pulse durations less than 1 ps, as taught by Mourou et al., to a method for treating a volume of tissue as per Latina, in order to better localize laser induced breakdown." Applicants

respectfully disagree and submit that such a combination is improper and even if combined, the combination thereof fails to disclose or suggest the claimed invention for at least the following reasons.

A. Latina does not teach the claimed method of treating a volume of tissue.

As described supra in reference to the Examiner's §102(e) rejection, Latina describes a method and apparatus suitable only for illumination of very small, individual target spots. This is not comparable to the feature of the claimed method of scanning over an extended volume of tissue, as recited in amended independent Claim 55 of the present application. Moreover, to effect treatment of anything but the tiniest areas of diseased tissue, Latina prescribes using a static "large target spot" that must be physically repositioned by the user (i.e., see col. 3, line 49 - col. 4, line 1 in Latina). Since Latina does not disclose and never considers utilizing a scanning approach, and in fact appears to teach away from the method and apparatus of the claimed invention by advocating manual repositioning of the treatment beam to a few target spots, Latina does not disclose or suggest the claimed method for treating a volume of tissue of Claim 55.

Accordingly, any alleged combination of the teachings of Latina with those of Mourou fails to redress this fundamental shortcoming of Latina, and does not result in the method of Claim 55 for treatment of a volume of tissue using thermal overload. Hence, Applicants respectfully submit that even if such a combination were proper, such combination would fail to arrive at the claimed invention.

B. Mourou does not teach the claimed method for treating a volume of tissue.

Instead of describing the claimed method for treatment of tissue using thermal energy (i.e., "thermal overload"), Mourou teaches a method of laser ablation (i.e., "laser induced breakdown") which requires careful *avoidance of thermal effects*. This fundamental difference is described below in depth.

Mourou is directed to laser induced breakdown (LIB) and the use of LIB to ablate patterns in various materials, as evidenced by the statement of the general object of the patent as:

> "It is a general object to provide a method to localize laser induced breakdown. Another object is to provide a method to induce breakdown in a preselected pattern in a material or on a material." (col. 1, lines 44 - 47 in Mourou)

The method utilized in Mourou to achieve LIB utilizes highly focused, ultrashort pulses (i.e., less than ca. 10 ps, as shown in Fig. 3 of Mourou). This preferred regime of pulse width is identified by measuring a "fluence breakdown threshold" (F_{th}) as a function of pulse width; the preferred regime comprises pulse widths less than those indicated by a certain inflection in the resulting curve, as describe by the following passage from Mourou:

> "An important aspect of the invention is the development of a characteristic curve of fluence breakdown threshold F_{th} as a function of laser pulse width specific to a material. Then identify on such curve, the point at which there is an abrupt, or distinct and rapid change or at least a discernable change in slope characteristic of the material. In general it is more desirable to operate past this point because of the more precise control of the laser induced breakdown (LIB) or ablation threshold." (col. 4, line 66 - col. 5, line 7)

The data represented in Fig. 3 of Mourou show that this threshold occurs at a pulse width in the range of about 1-10 ps, and that the preferred LIB regime is those pulse widths below that indicated by the arrow (i.e., at ca. 7 ps).

Mourou's use of this phenomenon as the basis for the invention therein is subsequently spelled out in the following passage from Mourou:

> "In experimental conditions with ... 200 fs pulses on gold (FIG. 3), the absorption depth is 275 Å with a diffusion length of 50 Å. In the case of nanosecond pulses the diffusion length, which is on the order of 10 μm (micron) in diameter, is much longer than the absorption depth, resulting in *thermal diffusion being the limiting factor in feature size resolution.* Empirical evidence for the existence of these two regimes is as exhibited in FIG. 3. Here both experimental and theoretical ablation thresholds are plotted as a function of pulse width. *An arrow at approximately 7 picoseconds* pulse width (designated herein as T or τ_p) delineates the point (or region closely bounding that point) at which the *thermal diffusion length* (l_{th}) is *equal to the absorption depth* (1/a). It is clear that for a smaller size spot a shorter (smaller) pulse is necessary. For spot size on the order of 1000 Å or less, pulse width on the order of 100 femtoseconds or less will be needed. It is clear from the figure that *this is the point at which the ablation threshold transitions from a slowly varying or nearly constant value as a function of pulse width to one that is dramatically dependent on pulse time.* This result is surprising.... The consequences of this for ultrafast laser pulses is that the energy is contained within the beam spot. In fact for energies at or near the threshold for ablation, the spatial profile of the laser beam will determine the size and shape of the region being ablated (FIGS. 4 and 5)." (col. 5, lines 26 - 54, emphasis added)

In summary, this passage teaches that when using relatively long pulses (i.e., longer than that indicated by the inflection point in Fig. 3), thermal effects dominate the interaction of pulsed laser light with matter. The consequence of such thermal interaction is larger interaction zones (i.e., micron-scale features for nanosecond pulses versus sub-micron features for sub-ps pulses).

Mourou further explains the reason why these thermal effects are important in the following passage:

> "Additional experiments were performed to measure [material removal using] a gold film.... In FIG. 4, the material removed is plotted as a function of fluence..... It is evident that by properly choosing the incident fluence, the ablated spot or hole can in principle be smaller than the spot size, R_s. This concept is shown schematically in FIG. 5. Although the data for a 150 fs pulse is shown in FIG. 4, this threshold behavior is exhibited in a wide range of pulse widths. However, *sub spot size ablation is not possible in the longer pulse regimes, due to the dominance of thermal*

diffusion as will be described below."- (col. 5, line 55 - col. 6, line 8, emphasis added)

Thus, Mourou describes a method for minimizing the ablation volume for LIB. As indicated by the preceding passage, a key to such minimization is careful avoidance of thermal effects.

The phenomenon described in Mourou is attributed to all materials, albeit with some minor differences related to specific physical characteristics of a particular material, as indicated by the following from the reference:

> "Opaque and transparent materials have common characteristics in the curves of FIGS. 3, 8, and 9.... [However] each curve is not necessarily the same since the materials differ. The physical characteristics of each material differ requiring a material specific analysis.... [Nonetheless] for any material, as the pulses get shorter laser induced breakdown (LIB) or ablation occurs only in the area where the laser intensity exceeds LIB or ablation threshold. There is essentially *insufficient time for the surrounding area to react thermally*. As pulses get shorter, vapor from the ablated material comes off after the deposition of the pulse, rather than during deposition, because the pulse duration is so short." (col. 10, line 21 - 44, emphasis added)

Accordingly, Mourou describes in this passage a universal method for ablation that has, as a central requirement, use of laser pulses of a certain duration and fluence selected so as to minimize the effects of various thermal processes.

That Mourou is concerned with avoidance of thermal effects that might interfere with the LIB process is further reinforced by the claims in the patent. For example, Claim 1 in Mourou is directed to a method for laser induced breakdown that utilizes highly focused laser pulses that are sufficiently short so as to avoid thermal effects that predominate under other conditions as recited below:

> Claim 1. A method for laser induced breakdown (LIB) of a material with a pulsed laser beam, the material being characterized by a relationship of fluence breakdown threshold versus laser pulse width that exhibits a rapid and distinct change in slope at a characteristic laser pulse width, said method comprising the steps of:

a. generating a beam of one or more laser pulses in which each pulse has a pulse width equal to or less than said characteristic laser pulse width; and

b. focusing said beam to a point at or beneath the surface of the material.

Accordingly, this claim and the supporting specification illustrate that Mourou teaches away from the subject of the claimed invention. Whereas amended independent Claim 55 of the present application is directed to a method of treatment based on thermal overload, the teachings in Mourou are directed in the opposite direction, to a method that avoids, at great cost and complexity, any thermal effects.[2]

For at least the above-stated reasons, Mourou fails to disclose or suggest the method of thermal overload of amended independent Claim 55 of the present application, and instead teaches away from such method. Moreover, any alleged combination of the teachings of Mourou with those of Latina fails to redress this fundamental shortcoming in Mourou, and does not result in the claimed method for treatment of a volume of tissue using thermal overload. Hence, Applicants respectfully submit that even if such a combination were proper, such combination would fail to arrive at the claimed invention.

---

[2] The inventors of the present application have worked with the types of lasers required to perform the LIB process described in Mourou. Such exotic lasers are typically extremely expensive (i.e., well over $100,000) and quite complicated. In contrast, the thermal overload processes described in the present application may be performed using much less expensive and far less complicated lasers, including solid state lasers (i.e., essentially very powerful versions of the diode lasers used in devices such as compact disk players).

C. The Combination of Latina with Mourou is not proper

In the Final Rejection, the Examiner contends that it would have been obvious to one of ordinary skill in the art to combine the teaching of Mourou and Latina. Applicants respectfully disagree.

It is well established that in order to combine references for a *prima facie* case of obviousness, there must be some teaching, suggestion or motivation to combine these references. No such teaching, suggestion, or motivation exists for this rejection.

More specifically, one skilled in the art, faced with the respective teachings of Latina and Mourou, would be required to overcome the fundamental contradictions of the two teachings, one concerning use of thermal effects (Latina) and one concerning avoidance of thermal effects (Mourou). Such contradiction teaches away from combining such references and such an intractable contradiction would prevent the skilled artisan from arriving at such hypothetical combination. In fact, it is only through picking pieces out of such references, while ignoring the remaining teaching in the references, that one could make such a hypothetical combination. As such a combination would be hindsight reconstruction, the combination is improper, and the rejection based thereon improper.

Therefore, for at least the above-stated reasons, the combination of these references is improper, and even if combined, fail to disclose or suggest the claimed invention. Hence, the claims are patentable over the cited references, and it is respectfully requested that this rejection be withdrawn.

VI. Conclusion

For at least the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

If any fee should be due for this Amendment, please charge our deposit account 50/1039.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

Date: October 6, 2004

Mark J. Murphy
Registration No. 34,225

COOK, ALEX, McFARRON, MANZO,
CUMMINGS & MEHLER, Ltd.
200 West Adams Street, Suite 2850
Chicago, Illinois 60606
(312) 236-8500
Customer No: 000026568